Journal of Pediatric Urology (2017) 13, 54.e1–54.e6

Blood pressure and urolithiasis in children

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Keywords
Kidney stones; Pediatrics; Hypertension; Urine calcium; Urine sodium

Received 8 March 2016
Accepted 1 July 2016
Available online 18 September 2016

Summary

Introduction
Urolithiasis is a condition that is most commonly found in adults, but is becoming increasingly prevalent in children. Little is known about the relationship between blood pressure (BP) and urolithiasis in children.

Objectives
The aim was to evaluate the relationship between urolithiasis and BP, and to determine the association of BP with 24-h urine parameters in children.

Methods
We retrospectively analyzed BP and 24-h urine data from children <18 years with and without urolithiasis from 2004 to 2015 at a single tertiary center. Children with a diagnosis of non-glomerular hematuria without history of urolithiasis were chosen as the control group. Non-stone formers were excluded if they presented with any abnormal 24-h urine data or kidney disease. Casual BP, BP index (BPi), and 24-h urine parameters were compared between groups using *t*-tests. Multiple regression analyses adjusting for age, sex and body mass index (BMI) z-score evaluated the association of BP with urolithiasis and urine electrolytes.

Results
The urolithiasis group ($N = 71$) was significantly older, taller and heavier than the non-stone former group ($N = 53$) (Table). Systolic BP and diastolic BP in stone formers were significantly greater than in non-stone formers, respectively ($p = 0.019$). Additionally, systolic BPi was significantly higher in the urolithiasis group ($p = 0.03$) but there was no significant difference in diastolic BPi ($p = 0.45$). Urolithiasis was a significant predictor of systolic BPi in the adjusted model ($\beta = 0.04$, 95% CI 0.001–0.07). In stone formers, systolic BP and systolic BPi were directly associated with 24-h urine sodium, oxalate/1.73 m^2, and uric acid (all $p < 0.05$). Urine calcium was not associated with any BP parameter.

Discussion
The findings are consistent with previous studies in adults that examined the correlation between blood pressure and kidney stones. The results of this study also showed that blood pressure was positively associated with urine sodium, oxalate, and uric acid. Interestingly, contrary to adult literature, our hypothesis which postulated that blood pressure would be associated with an increase in urine calcium was not supported by our findings. The small sample size is a study limitation and the use of healthy controls as a comparison would have been ideal.

Conclusions
Blood pressure was directly associated with urolithiasis children. Greater BP values were also associated with abnormalities in 24-h urine oxalate, uric acid, and sodium values. Interestingly, BP was not associated with urine calcium in this population.

Table Stone formers vs. non-stone formers.

Characteristics	Stone formers ($N = 71$)	Non-stone formers ($N = 53$)	p
Male	34 (47.9)	34 (64.2)	0.07
Age (years)	11.2 ± 4.1	9.2 ± 3.5	0.005
Body mass index z-score	0.57 ± 2.68	0.68 ± 1.19	0.78
Systolic blood pressure (mmHg)	109.4 ± 14.7	103.0 ± 12.7	0.01
Diastolic blood pressure (mmHg)	65.0 ± 8.3	61.4 ± 8.6	0.02
Systolic blood pressure index	0.89 ± 0.10	0.86 ± 0.10	0.03
Diastolic blood pressure index	0.81 ± 0.10	0.78 ± 0.35	0.45

Note. Values are mean ± SD or *N* (%).

http://dx.doi.org/10.1016/j.jpurol.2016.07.017

Introduction

Urolithiasis, or the formation urinary calculi, is a condition that is highly recurrent and associated with morbidity [1]. Urolithiasis is most commonly found in middle-aged adults, but it is becoming increasingly prevalent in children [1]. From 1950 to 1990, urolithiasis accounted for 1 in 7600 to 1 in 1000 pediatric hospitalizations in the United States [1]. In a more recent study, which retrospectively examined pediatric hospitalizations in the United States between 2002 and 2007, urolithiasis had become significantly more prevalent and accounted for 1 in 685 pediatric hospitalizations [1].

Hypercalciuria and increased dietary sodium intake are known risk factors for urolithiasis in adults and children [2–4]. Further studies have determined that urine calcium levels are directly correlated with blood pressure and salt intake in adults [5–7]. Additionally, recent epidemiologic studies have demonstrated an independent association between hypertension and urolithiasis in adults [4,8–11]. It is unclear which of these variables precedes the other, and the specific mechanisms are still being unraveled.

Currently, there is little known about the relationship between blood pressure and urolithiasis in children. Thus, the main objectives of this study were to evaluate the relationship between urolithiasis and blood pressure, and to determine the association of blood pressure with 24-h urine parameters in children. We hypothesized that urolithiasis would be directly associated with blood pressure in children. In addition, we postulated that blood pressure would be associated with greater excretion of calcium and sodium in the urine. A better understanding of these risk factors will shed light on the epidemiology of this disease in children, and assist physicians in preventing and treating urolithiasis.

Materials and methods

Study population and design

Seventy-one children with a diagnosis of urolithiasis evaluated in the Pediatric Nephrology and Pediatric Urology clinics at the Cohen Children's Medical Center of New York between 2004 and 2015 were included in this retrospective study as part of the stone former group. All participants had confirmation of urolithiasis by ultrasound or computed tomography (CT) scan, and had a 24-h urine collection (Litholink Corporation, Chicago, IL, USA) performed shortly after their original visit. Children <18 years old who had height, weight, and casual blood pressure measured during a nephrology/urology office visit within 3 months of their diagnosis of urolithiasis were included (patients with active pain at the time of the visit were excluded as pain is known to affect blood pressure). Given the retrospective nature of this study and the lack of access to 24-h urine studies in healthy children, 53 children with a diagnosis of non-glomerular hematuria (microhematuria or gross hematuria), confirmed on microscopy by a nephrologist without history of urolithiasis who completed a 24-h urine collection, were chosen as the control group. Children were excluded from the non-stone former group if they presented with any abnormal 24-h urine metric or were found to have any type of kidney disease (e.g., polycystic kidneys, dysplastic kidney, glomerulonephritis, etc.). Two hundred and sixty children (stone formers and non-stone formers) with 24-h urine studies did not meet the inclusion criteria and were excluded from the study. This study protocol was approved by the Institutional Review Board of the Northwell Health System.

Twenty-four-hour urine values were recorded, which included urine volume, supersaturation of calcium oxalate, urine calcium, urine oxalate, urine citrate, supersaturation of calcium phosphate, pH, supersaturation of uric acid, urine uric acid, urine sodium, urine potassium, urine magnesium, urine phosphorus, and urine creatinine. Urine calcium, phosphorus, and potassium values were adjusted for weight (kg) in children <16 years of age and urine oxalate and uric acid values were adjusted for body surface area 1.73 m^2. In addition, demographic information, height, weight, and casual blood pressure from the corresponding office visit were recorded. Blood pressure was measured from the right arm using an oscillometric device during an office visit while the patient was seated after 5 min of rest. To allow for comparison across the age groups, body mass index (BMI) *z*-scores were calculated, and blood pressure readings were converted to blood pressure indices. The blood pressure index (BPi) was calculated by dividing blood pressure by the age, sex and height specific 95th percentiles for systolic and diastolic blood pressure [12]. A BPi >1 indicated hypertension.

Statistical analysis

Descriptive analyses included means and standard deviations (SD) of continuous variables and distributions of categorical variables. Demographic and clinical variables, systolic and diastolic blood pressure were compared between stone formers and non-stone formers using independent samples *t*-test, Mann–Whitney, or chi-square analysis, as appropriate. The correlation between blood pressure and urine electrolytes was determined using Pearson/Spearman correlation coefficients. Multiple linear regression models to assess urolithiasis as a potential predictor of blood pressure were done adjusting for sex, age, and BMI *z*-score (variables chosen a priori). Multiple linear regression models were used to determine the relationship between urine electrolytes and blood pressure in the stone former group only. One-time stone formers were also compared with recurrent stone formers. The overall level of significance was set at 0.05, using two-tailed tests of hypotheses. Statistical analyses were done using the SPSS 22.0 (IBM Inc.) statistical package.

Results

Stone formers and non-stone formers

Blood pressure, demographic, and urine concentration data for the stone former (age range 3–17 years) and non-stone former (age range 3–15 years) groups are summarized in Table 1. The urolithiasis group was significantly older, taller, and heavier than the non-stone former group; however, BMI *z*-scores were not significantly different. The average absolute systolic and diastolic blood pressures in stone formers were significantly greater than the non-stone